double bonds, often as alkenyl substituents, are present in the starting material and remain in the product of such reactions.

Rather than demonstrating a lack of enablement, the Examiner's recognition of the possibility of untoward outcomes in some reactions involving various of the schemes provided in the specification demonstrates that a worker of ordinary skill (a Ph.D. chemist with several years of laboratory bench experience, according to the Examiner) would also recognize the need to modify the reactants and reactions to prevent such untoward outcomes. It is respectfully submitted that the ordinary artisan in this art would not only recognize (as the Examiner has) the potential difficulties, but would know how to circumvent these problems.

The Examiner further notes that "the palladium carbon reaction is notorious for reducing double bonds." Certainly if "the palladium carbon reaction is notorious for reducing double bonds," the skilled artisan would know this, and would modify the synthesis accordingly, e.g., by routine adaptation of one of the other schemes provided. Similarly, if the compound to be synthesized would contain multiple instances of a functional group and only one was desired to react with a reagent, the skilled artisan would modify any synthesis steps accordingly.

For example, in the case of the nitro substituents cited by the Examiner, the worker of ordinary skill would know a reduction reaction could be done using precursor starting material having only one nitro substituent -- and hydrogen(s), for example, at locations where other nitro groups are desired -- followed by nitration of the product of the reduction. In addition, many functional groups are susceptible of modification and/or protection steps well known to those of ordinary skill in the art at the time of the filing of the application (See e.g., T.W. Greene and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, 3rd Ed., John Wiley and Sons (1999) that provide further avenues for the skilled worker, via routine experimentation, to successfully cope with the difficulties noted by the Examiner.

In citing the particular instances where one or the other of the presented schemes would require modification in order to produce a claimed compound, the

Examiner seems to be arguing that every one of the disclosed synthetic schemes must enable the synthesis of all of the claimed compounds without any need for experimental variation. This is not the standard for enablement. The question is not whether a worker, blindly following the schemes would be able to synthesize the full scope of claimed compounds. Rather, it is whether a worker of ordinary skill (whom, applicants would argue, is not only a Ph.D. chemist with several years of laboratory bench experience, but is a Ph.D. synthetic medicinal chemist with several years of synthetic medicinal chemistry laboratory bench experience) would, by the application of the skills and knowledge attributable to such an artisan, be able to synthesize the claimed compounds without undue experimentation, i.e., with only routine experimentation.

> the applicant's specification must enable one of ordinary skill in the art to practice the full scope of the claimed invention. That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments" (internal citation omitted).
> *AK Steel Corp. v. Sollac*, 68 USPQ2d 1280, 1287 (Fed. Cir. 2003)

By not addressing this question of routine experimentation with any particularity in regard to the reaction conditions cited in making this rejection, the Examiner has failed to make a proper *prima facie* showing of lack of enablement. Reconsideration and withdrawal of this rejection under 35 U.S.C. §112 is earnestly solicited.

Claim Rejections – 35 U.S.C. §102(b)

Claim 1 has been rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Christensen, et al., (J. Org. Chem., 1971, 36(17), 2462), which rejection is respectfully traversed. As the Examiner noted in the Office Action, the cited CA reference # 29939-35-3 compound "contains a pyrimidine with a phenyl in the 2 position..." This phenyl in the reference compound is unsubstituted, however, while rejected Claim 1 recites that the corresponding phenyl "is mono-, di-, or tri-substituted." Thus the claim is not anticipated by the reference compound and withdrawal of the rejection is respectfully requested.

Claims 3, 5, 15, and 16 have been rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Kameko, (JP 10237477; 1998), which rejection is respectfully traversed. Both independent claims 3 and 15 (and dependent claims 5 and 16 by their dependency therefrom) comprise the restriction "with the proviso that not both R_1 and R_3 are hydrogen," while the reference compound has hydrogens at the positions corresponding to both R_1 and R_3. Thus these claims are not anticipated by the reference compound and withdrawal of the rejection is respectfully requested.

Claim Rejections – 35 U.S.C. §103

Claims 1, 3-22, 30, 35, 39-64 and 69 have been rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Kleemann et al. (US 5,849,758), in view of Hoefle et al. (US 4,716,175), which rejection is respectfully traversed.

As noted by the Examiner "the 2-arylpyrimidine compounds [of Kleemann et al.] were synthesized and tested to be used as a herbicidal agent. " The Hoefle et al., patent discloses "certain substituted amides of α-substituted or α,α-disubstituted alkanoic and alkenoic acids which inhibit acyl-coenzyme A:cholesterol acyltransferase (ACAT), pharmaceutical compositions containing these compounds, and a method of inhibiting intestinal absorption of cholesterol. " (Hoefle et al., column 1, lines 12-18.) The Examiner has not shown how cholesterol might be involved in the actions of herbicides, nor is any such involvement believed to exist. Plants contain little cholesterol and no intestines, so there is no reason why "inhibiting intestinal absorption of cholesterol" would be expected to have any herbicidal effects. Furthermore, while the Examiner avers that "[w]ithin Hoefle et al. (col. 2) , a similar core structure is present," the alleged "similar core structure" that the Examiner cites in Hoefle is rather one of three alternate "B" substituents of Hoefle's core formula set forth at column 2, lines 1-7.

The Examiner has not shown any reason why a person of ordinary skill in the herbicide arts would look to an alternate substituent of a group of inhibitors of acyl-coenzyme A:cholesterol acyltransferase as a template for the modification of herbicidal

compounds in expectation of enhanced herbicidal activity. Thus there is not any reason for a worker of ordinary skill, in the Examiner's words, "to try replacing the aryloxy group in the 4-position of the Kleemann patent with an alkyloxy group such as the one discussed in the Hoefle patent at the same position of the pyrimidine ring in an attempt to obtain a compound or composition which possesses enhanced activity and to afford a positive benefit from the replacement." Nor has the Examiner made any showing that there might be a reasonable expectation of success for improved herbicidal activity of compounds resulting from such replacements. The rejection of these claims under 35 U.S.C. §103(a) is therefore improper and its withdrawal is respectfully requested.

Conclusion

In view of the above, Applicants respectfully request withdrawal of the pending rejections and objections and allowance of the application.

Although it is not believed that any additional fees are needed to consider this submission, the Examiner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

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Respectfully submitted,

By _____

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